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**REVIEW MANAGEMENT**

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**Process for Handling Pediatric Exclusivity**

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**PURPOSE** This MAPP describes the process for handling pediatric exclusivity. For questions regarding the policy or procedures, please send an email to "PDIT."

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## BACKGROUND

Section 111 of Title I of the Food and Drug Administration Modernization Act of 1997 (the Modernization Act), signed into law by President Clinton on November 21, 1997, created section 505A of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. 355a). Section 505A permits certain applications to obtain an additional six months of marketing exclusivity (pediatric exclusivity) if, in accordance with the requirements of the statute, the sponsor submits requested information relating to the use of the drug in the pediatric population.

Section 505A of the Act includes the following elements that must be met for a drug to qualify for pediatric exclusivity. Relevant sections of FDA's guidance for industry *Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act* are identified at the end of each element.

- The drug, if approved (section 505A(c)), must appear on the "List of Approved Drugs for Which Additional Pediatric Information May Produce Health Benefits in the Pediatric Population." Unapproved drugs, as defined in this MAPP, do not need to appear on the list (section 505A(a)). (Refer to sections II.B.1 and V. C of the guidance.)
- The Agency must issue a Written Request for pediatric studies under section 505A(a) or 505A(c). (Refer to section IV of the guidance.)
- The reports of studies should be submitted after the Agency makes the Written Request. Pediatric study reports submitted to a new drug application (NDA) after November 20, 1997, and before July 1, 1998 (the date of issuance of the guidance *Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act*), may be considered responsive to a Written Request. (Refer to section III.C of the guidance.)
- Submitted studies must respond to (i.e., satisfy the conditions of) the Written Request (section 505A(d)(2) and (3)). (Refer to section IX of the guidance.)
- The studies must be conducted in accordance with a written agreement (section 505A(d)(1) and (2)) or, if there is no written agreement, in accordance with commonly accepted scientific principles (section 505A(d)(3)). (Refer to sections VI and VII of the guidance.)

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- The reports of the studies must be submitted in accordance with the Agency's requirements for filing (section 505A(d)). (Refer to section VIII of the guidance.)
  - The Agency must accept the reports of studies (section 505A(d)). Acceptance means the Agency has determined that the studies were conducted in accordance with the original Written Request and either a written agreement if one existed or commonly accepted scientific principles if no written agreement existed, and were submitted in accordance with FDA's requirements for filing (section 505A(d)(2) and (3)). (Refer to section IX of the guidance.)

Section 505A became effective on November 21, 1997, and will sunset on January 1, 2002.

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## REFERENCES

- Food and Drug Administration Modernization Act of 1997 (Pub. L. 105-115) (Modernization Act), November 21, 1997.  
<http://www.fda.gov/cder/guidance/105-115.htm#SEC. 111>
  - *Qualifying for Pediatric Exclusivity Under Section 505A of the Federal Food, Drug, and Cosmetic Act*, June 1998.  
<http://www.fda.gov/cder/guidance/2414fnl.htm>
  - “List of Approved Drugs for Which Additional Pediatric Information May Produce Health Benefits in the Pediatric Population” (21 U.S.C. 355a(b)). Refer to Docket 98N-0056 for the current list.  
<http://www.fda.gov/cder/pediatric/peddrugsfinal.pdf>
  - *Approved Drug Products with Therapeutic Equivalence Evaluations* (Orange Book). <http://www.accessdata.fda.gov/ob/default.htm>
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## DEFINITIONS

- **Active Moiety.** “The molecule or ion, excluding those appended portions of the molecule that cause the drug to be an ester, salt (including a salt with hydrogen or coordination bonds), or other noncovalent derivative (such as a complex, chelate, or clathrate) of the molecule, responsible for the physiological or pharmacological action of the drug substance” (21 CFR

314.108(a)).

- **Approved drug.** For purposes of this MAPP, an approved drug is an active moiety that is approved for use in adults and/or for use in a part of the pediatric population for an indication that occurs in the pediatric population.
- **Pediatric Exclusivity Board.** A group comprising members from the Office of Review Management, Office of Generic Drugs, Regulatory Policy Staff, and Office of the Chief Counsel that makes recommendations to the Deputy Center Director (Review Management) on pediatric exclusivity determinations. This board is chaired by the Deputy Center Director (Review Management).
- **Pediatric Implementation Team (PdIT).** A group comprising members from the Office of Review Management, Office of Generic Drugs, and Regulatory Policy Staff that provides assistance to CDER staff in implementing 505A of the Act. This team is chaired by the Director, Office of Drug Evaluation IV.
- **Pediatric study.** At least one clinical investigation (that, at the Agency's discretion, may include pharmacokinetic studies) in pediatric age groups in which a drug is anticipated to be used (section 505A(g)).
- **Proposed pediatric study request.** A submission by the sponsor or an interested party that proposes a Written Request and addresses all of the terms in Attachment B.
- **Sponsor.** Any person who submits an application or who takes responsibility for and initiates a clinical investigation.
- **Unapproved drug.** For purposes of this MAPP, an unapproved drug is an active moiety that is not yet approved (i.e., is pending) under section 505 of the Act or is not yet an approved indication of an approved active moiety.
- **Written Request.** A specific letter (see Attachment A) from FDA to the sponsor, signed by the appropriate Director(s) of the Office of Drug Evaluation responsible for regulation of the product(s), in which the Agency requests submission of certain studies to provide needed information on use in the pediatric population. Other informal requests for studies (e.g., agreements to perform Phase 4 studies or other communications concerning pediatric studies) are not official Written Requests.

- **Written agreement.** A document (see Attachment E) signed by FDA and the sponsor that sets forth a plan for addressing all of the items in the Written Request including what will be necessary to meet the study objective(s). The agreement should state that the results of the studies as conducted should be adequate to address the objective of the studies as set forth in the Written Request (section 505A(d)). The written agreement should include protocols for the studies to be conducted and/or procedures for review of the protocols. The protocol should meet the requirements of 21 CFR 312.23(a)(6). Where required, adequate and well-controlled studies should meet the requirements of 21 CFR 314.126. A written agreement for the conduct of pediatric studies may be modified by written agreement between the Agency and the sponsor.

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## POLICY

- FDA will work with sponsors of unapproved and approved drugs to ensure that studies are conducted that produce information that may provide a health benefit in the pediatric population.
- The Written Request will be issued to a new drug application (NDA) when an NDA exists. If no NDA exists, the Written Request will be issued to an investigational new drug application (IND).
- Generally, FDA's Written Request will address the issues outlined in Attachment B.
- The Written Request should request all pediatric information needed for a particular active moiety except when there is a scientific justification for asking only for a particular use or pediatric age group.
- Separate Written Requests should be issued for unapproved and approved drugs for a particular active moiety.
- The Agency will use all sources of information to develop the Written Request and will consider any proposed pediatric study requests in developing the Written Request.
- FDA may issue a Written Request for pediatric studies based on an outside proposal or on its own initiative.
- FDA's Written Request will include a provision for amending a Written

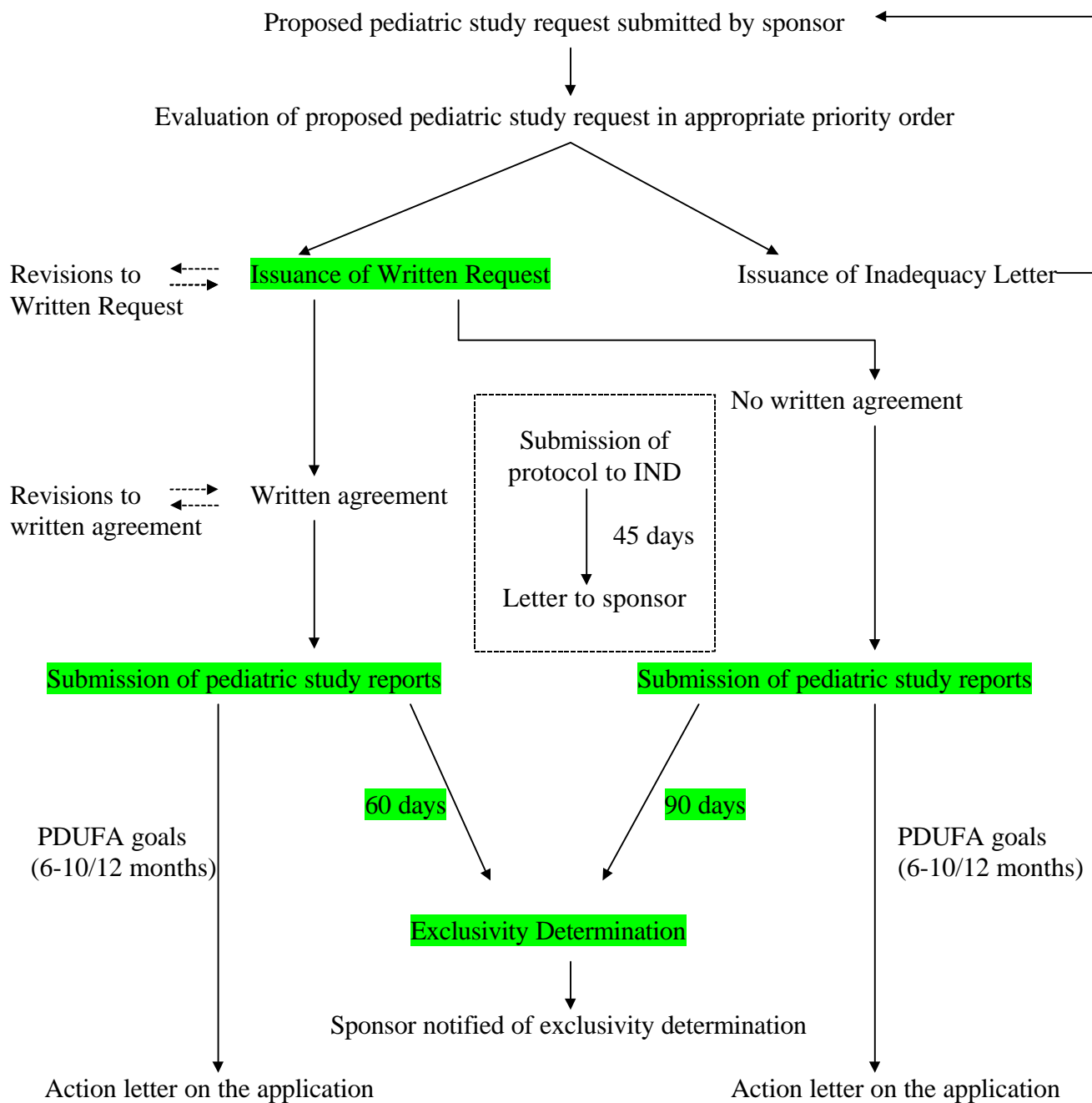
Request. FDA will communicate any agreed upon changes to the Written Request in writing to the sponsor in accordance with the provision for amending the Written Request. Requests from sponsors for amendments to the Written Request should be submitted in writing.

- To facilitate the Agency's issuance of a Written Request, interested persons are strongly encouraged to submit proposed pediatric study requests. The submission should be clearly marked with the header PROPOSED PEDIATRIC STUDY REQUEST. At a minimum, any proposed pediatric study request should address the issues identified in Attachment B.
- FDA recommends that persons to whom Written Requests are issued reach a signed written agreement with FDA for the conduct of pediatric studies.
- Pediatric protocols submitted for pediatric exclusivity studies are considered special protocols and will be processed within 45 days. Pediatric protocols do not need to meet any other elements (e.g., the sponsor does not need to have an End-of-Phase II meeting) to qualify as special protocols.

## PROCEDURES

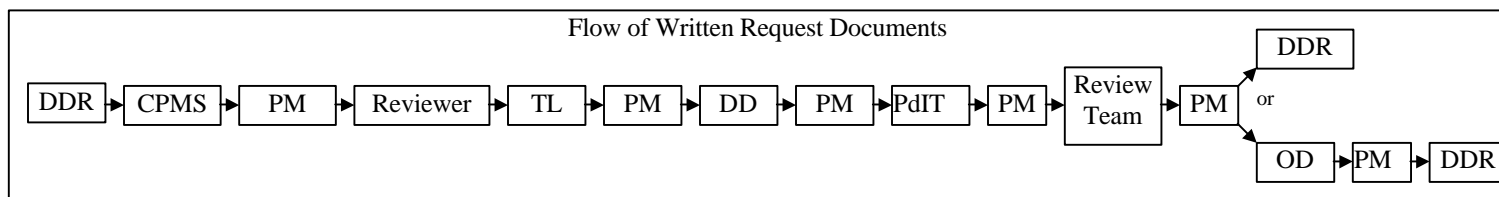
The following diagram outlines the process for handling pediatric exclusivity documents.

NOTE: Highlighted areas are steps that must occur.



## RESPONSIBILITIES

### ◇ Issuing Written Requests and Changes to Written Requests



#### **Division Document Room (DDR)**

Within 3 working days of receipt of a submission marked “PROPOSED PEDIATRIC STUDY REQUEST” or “PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES”

- Logs receipt of the submission into the Pediatric Exclusivity Tracking System
- Forwards the submission to the Chief, Project Management Staff.

Within 3 working days of receipt of the signed Written Request letter, Revised Written Request letter, or Inadequacy Letter from the Project Manager

- Logs the data into the Pediatric Exclusivity Tracking system.
- Mails the Written Request or Inadequacy Letter and forwards copies as appropriate.
- Files copies of the documents in the appropriate applications.

#### **Chief, Project Management Staff (CPMS)**

- Prioritizes review of proposed pediatric study requests based on *the Table on Review Priority* on the next page.
- Forwards the proposal to the appropriate Project Manager.
- Informs the Project Manager of the need for consultation with other new drug review divisions based on recommendations by the PdIT.

**Table on Review Priority**

	Drugs on the Priority Section of the List		Drugs Not on the Priority Section of the List		Unapproved Drugs
	Patent or Exclusivity expiration on or before 03/31/99	Patent or Exclusivity expiration <i>not</i> on or before 03/31/99	Patent or Exclusivity expiration on or before 03/31/99	Patent or Exclusivity expiration <i>not</i> on or before 03/31/99	
Proposed Pediatric Study Request submitted on or before 08/31/98	1	2	3	4	2
Proposed Pediatric Study Request <i>not</i> submitted on or before 08/31/98	2		4		2

This means:

1. Each ORM Review Division will first process proposed pediatric study requests submitted on or before August 31, 1998, for approved drugs that appear in the priority section of the list for which any marketing exclusivity (orphan or Hatch-Waxman) or listed patent period expires on or before March 31, 1999.
2. Each ORM Review Division will next process:
  - a. any other proposed pediatric study requests for approved drugs that appear in the priority section of the list, and
  - b. proposed pediatric study requests submitted for drugs that are not yet approved.
3. Each ORM Review Division will then process proposed pediatric study requests submitted on or before August 31, 1998, for approved drugs that appear in the nonpriority section of the list for which any marketing exclusivity (orphan or Hatch-Waxman) or listed patent period expires on or before March 31, 1999.
4. Each ORM Review Division will finally process any other proposed pediatric study requests for approved drugs that appear in the nonpriority section of the list.

Generally, each ORM Review Division will initiate review of proposed pediatric study requests within each priority in the order the proposals are received by the appropriate new drug review division as indicated by the official FDA document room receipt stamp.

**Project Manager (PM)**

- Upon receipt of the proposed pediatric study request (or changes to the request) from the CPMS, forwards the proposed pediatric study request (or changes to the request) to the appropriate reviewer(s).
- Upon receipt of the Written Request review and checklist from the Team Leader, prepares a Written Request letter (Attachment A) or Inadequacy Letter (Attachment D) based on the Review Team's decision.
- Obtains appropriate clearances on the draft letter from the Reviewers and Team Leader, as needed and forwards the Written Request review, checklist, and Written Request or Inadequacy Letter to the Division Director.
- Upon receipt of the Written Request or Inadequacy Letter from the Division Director, forwards a copy to the Pediatric Implementation Team (PdIT).
- Upon receipt of the recommendations of the PdIT on the Written Request or Inadequacy Letter, revises the letter accordingly and obtains all necessary signatures. Forwards the Inadequacy Letter to the DDR and the Written Request letter to the Office Director.
- Upon receipt of the signed Written Request letter from the Office Director, forwards the completed package to the DDR.

**Medical Officer/Biopharm/Statistical Reviewers**

Reviews the proposed pediatric study request (or amended request) and initiates any negotiations on needed changes with the sponsor through the Project Manager.

- Determines whether the proposal contains the necessary elements by completing Attachment B. If the appropriate items are not addressed, an Inadequacy Letter may be issued or additional discussions may be held with the sponsor to complete the proposal
- If the proposed pediatric study request contains all of the elements identified in Attachment B but does not call for the type of information that is needed in the Agency's best judgment, the review team may (1) prepare a Written Request that reflects the best judgment of the Agency or (2) ask the sponsor to submit a new proposal that addresses the concerns outlined by the Agency.

- If the proposed pediatric study request contains all appropriate elements identified in Attachment B and meets the Agency's best judgment for the type of studies that are needed to provide information in the pediatric population, the Review Team prepares a Written Request review taking into consideration the proposed pediatric study request submitted by the sponsor and any other information.
- Forwards a copy of the Written Request review and checklist to the Team Leader.

**Team Leader (TL)**

- Reviews and indicates concurrence with the Written Request review and checklist, or works with the Review Team to bring the documents into conformance with regulatory, policy, and scientific requirements.
- Forwards the Written Request review and checklist to the Project Manager.

**Division Director (DD)**

- Reviews and indicates concurrence with the Written Request review (or amended request), checklist, and Written Request or Inadequacy Letter, or works with the review team to bring the documents into conformance with regulatory, policy, and scientific requirements.
- Signs the Inadequacy Letter, if appropriate, and forwards to the Project Manager.
- Forwards the Written Request review (or amended Written Request), checklist, and Written Request letter to the Project Manager.

**Pediatric Implementation Team (PdIT)**

- Reviews the Written Request or Inadequacy Letter and forwards any recommendations to the Project Manager.

**Office Director (OD)**

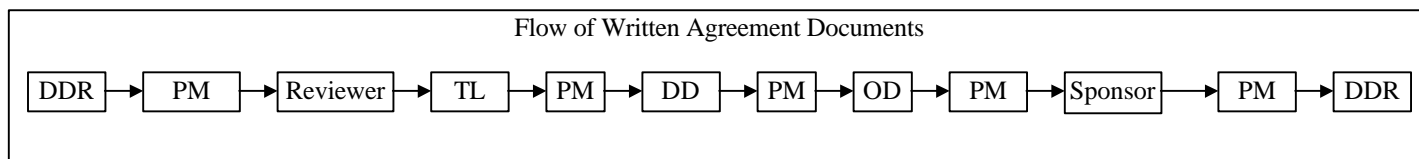
- Reviews and indicates concurrence with the Written Request review (or amended request), checklist, and Written Request letter by signing the letter, or works with the review team to bring the documents into conformance with regulatory, policy, and scientific requirements, as necessary.
- Forwards the completed documents to the Project Manager.

◇ **Coordination of Multi-division Written Requests****Pediatric Implementation Team (PdIT)**

- On a weekly basis, identifies all new drug review divisions regulating the active moieties for which proposed pediatric study requests have been submitted.
- Informs all appropriate Chiefs, Project Management Staff, Division Directors, and Office Directors of receipt of proposed pediatric study requests and the need to coordinate efforts.

**Review Division to which proposed pediatric study request was submitted**

- Takes the lead in preparing the Written Request.
- Ensures proper sign-off from all appropriate Office and Division authorities.

◇ **Establishing A Written Agreement****Division Document Room**

Within 3 working days of receipt of a submission marked “PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES” or “CHANGES TO WRITTEN

**AGREEMENT FOR PEDIATRIC STUDIES,”**

- Logs receipt of the submission into the Pediatric Exclusivity Tracking system.
- Forwards the submission to the appropriate Project Manager.

Within 3 working days of receipt of the written agreement signed by the sponsor and Office Director from the Project Manager

- Logs the written agreement signed by both parties into the Pediatric Exclusivity Tracking System.
- Mails one original copy to the sponsor and files the other original copy in the application. Copies of the agreement should be distributed appropriately.

**Project Manager**

- Upon receipt from the DDR, forwards the proposed (or amended) written agreement to the appropriate Reviewer(s).
- Upon receipt of the draft written agreement from the Team Leader, prepares two copies of the final written agreement in accord with Attachment E and based on the Review Team’s and sponsor’s understandings, and obtains appropriate clearances from the Review Team and Team Leader before forwarding the two copies to the Division Director.
- Upon receipt from the Division Director, forwards both copies to the Office Director.
- Upon receipt from the Office Director, obtains the sponsor’s signature on both copies of the final written agreement (signature may be obtained via facsimile).
- After obtaining the sponsor’s signature, forwards both copies of the written agreement signed by both the Office Director and the sponsor to the Division Document Room.

**Medical Officer/Biopharm/Statistical Review Team**

- Reviews the proposed written agreement and initiates any negotiations on

needed changes with the sponsor through the Project Manager.

- Prepares a draft written agreement and forwards it to the Team Leader.

#### **Team Leader**

- Reviews and indicates concurrence with the written agreement, or works with the Review Team to bring the document into conformance with regulatory, policy, and scientific requirements.
- Forwards the written agreement to the Project Manager.

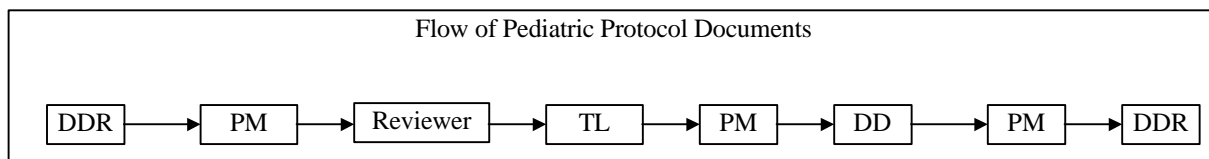
#### **Division Director**

- Reviews and indicates concurrence with the written agreement, or works with the Review Team to bring the document into conformance with regulatory, policy, and scientific requirements.
- Forwards the written agreement to the Project Manager.

#### **Office Director**

- Reviews and indicates concurrence with the written agreement by signing it, or works with the Review Team to bring the document into conformance with regulatory, policy, and scientific requirements, as necessary.
- Forwards the completed documents to the Project Manager.

#### ◇ **Processing Pediatric Protocols**<sup>1</sup>



<sup>1</sup> Pediatric protocols submitted for pediatric exclusivity studies are considered special protocols and will be processed within 45 days.

**Division Document Room**

Within 2 working days of receipt of a submission marked PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY

- Logs receipt of the submission into the Pediatric Exclusivity Tracking system.
- Forwards the submission to the appropriate Project Manager.

Within 3 working days of receipt of the letter signed by the Division Director,

- Logs information into the MIS system.
- Issues the letter signed by the Division Director and distributes copies, as appropriate.

**Project Manager**

- Tracks the pediatric protocol and any necessary communications regarding the protocol.
- Upon receipt of the protocol from the DDR, forwards the submission to the appropriate reviewer(s).
- Upon receipt of the review, prepares a letter for the Division Director's signature communicating the Review Team's findings to the sponsor.
- Upon receipt of the signed letter from the Division Director, forwards the documents to the DDR.

**Medical Officer/Biopharm/Statistical Review Team**

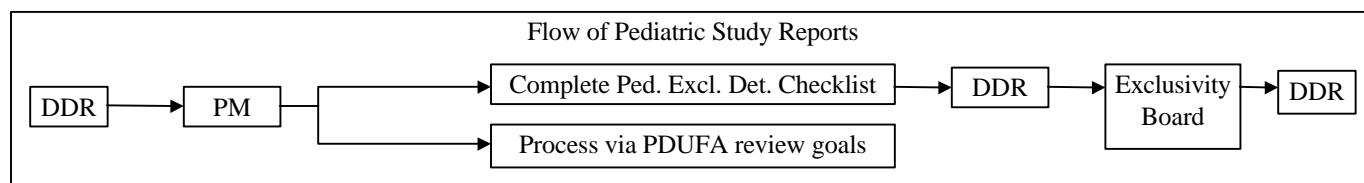
- Reviews the protocol to ensure it complies with the terms stated in the Written Request and written agreement, if there is one.
- Forwards the review to the Team Leader.

**Team Leader**

- Reviews and concurs with the review, or works with the Review Team to bring the document into conformance with regulatory, policy, and scientific requirements.
- Forwards the review to the Project Manager.

**Division Director**

- Reviews the documents and signs the letter, or works with the Review Team to bring the document into conformance with regulatory, policy, and scientific requirements.
- Forwards the signed documents to the Project Manager.

**◇ Processing Submitted Pediatric Study Reports****Division Document Room,**

Within 3 working days of receipt of a submission marked “SUBMISSION OF PEDIATRIC STUDY REPORT -- PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED”

- Logs the submission into the Pediatric Exclusivity Tracking system and forwards the material to the Project Manager.

Within 3 working days of receipt of the Pediatric Exclusivity Determination Checklist,

- Enters the appropriate data from the Pediatric Exclusivity Determination Checklist into the Pediatric Exclusivity Tracking System
- Forwards the checklist to the Pediatric Exclusivity Board, HFD-002.

**Project Manager**

- Upon receipt of the pediatric study reports, immediately notifies the Pediatric Implementation Team (via email to “PDIT”) of the submission and that a pediatric exclusivity determination is in progress.
- In consultation with the review team
  - \* For those drugs where a written agreement was established: within 30 calendar days of receipt of the submission, completes Part I of the Pediatric Exclusivity Determination Checklist (Attachment F) and forwards it to the Division Document Room.
  - \* For those drugs where no written agreement was established: within 60 calendar days of receipt of the submission, completes Part I of the Pediatric Exclusivity Determination Checklist (Attachment F) and forwards it to the Division Document Room.
- Processes submission of the reports in accordance with normal review procedures.

◇ **Granting/Denying Pediatric Exclusivity**

**Pediatric Exclusivity Board**, within the required 60 (when there is a written agreement) or 90 (when no written agreement exists) calendar days of submission of the pediatric study reports,

- Recommends pediatric exclusivity be granted or denied and determines the patent(s) and exclusivity that will be affected.
- Notifies the Project Manager in the ODE Review Division, Director, Division of Labeling and Program Support, OGD, and the Division of Data Management Services of the exclusivity determination.
- Enters the decision into the Pediatric Exclusivity Tracking System.
- Forwards the completed Pediatric Exclusivity Determination Checklist to the Division Document Room.

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**Deputy Center Director (Review Management)**

- Grants or denies pediatric exclusivity based on the pediatric exclusivity board's recommendations.

**Division Document Room**, within 3 working days of receipt of the completed Pediatric Exclusivity Determination Checklist from the Pediatric Exclusivity Board,

- Files the form in the appropriate application and division file and forwards a copy to the Project Manager.

**Project Manager, ODE Review Division**, within 3 calendar days of notification from the Exclusivity Board,

- Informs the sponsor of the pediatric exclusivity determination via phone.

**Division of Data Management Services**

- For approved products, publishes granted pediatric exclusivity determinations in the next supplement to the Orange Book.
- For unapproved drugs, publishes the granted pediatric exclusivity determination upon approval of the application in the appropriate supplement to the Orange Book.

◇ **Approving or Filing 505(j) and 505(b)(2) Applications**

**Office of Generic Drugs (OGD) and ODE Review Divisions, prior to approval of a 505(j) or (b)(2) application OR filing a 505(j) or (b)(2) when NCE exclusivity exists**

- Checks the Pediatric Exclusivity Tracking System to determine if a Written Request for pediatric studies has been made.
- If a Written Request has been made, the Project Manager or responsible official in OGD or the ODE Review Division checks with the Chief, Project Management Staff in the ODE Review Division(s) or PdIT to determine if pediatric studies have been submitted. If pediatric studies have been submitted and exclusivity or patent protection has not yet expired, the 505(b)(2) or (j)

application should not be approved or accepted, as appropriate, prior to the pediatric exclusivity determination or before the expiration of 90 days, whichever comes first. NOTE: For studies conducted pursuant to a written agreement, the Agency must determine within 60 days whether the studies were conducted in accord with the written agreement.

- Once the exclusivity determination is made, the OGD or New Drug Review Division, as appropriate, may approve or file 505(j) or (b)(2) applications after the expiration of all existing listed patent and exclusivity protections that affect the 505(j) or (b)(2) application.
- 

#### **EFFECTIVE DATE**

This MAPP is effective upon date of publication.

### Sample Letter for a Written Request for Pediatric Studies

NDA/IND APPLICATION NUMBERS

SPONSOR

Attention: CONTACT, TITLE

ADDRESS

Dear CONTACT:

Reference is made to your Proposed Pediatric Study Request submitted on INSERT DATE for DRUG PRODUCT(S) to APPLICATION NUMBER(S).

To obtain needed pediatric information on GENERIC DRUG NAME, the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act (the Act), that you submit information from the following STUDY/STUDIES:

COMPLETE AND INCLUDE ALL APPROPRIATE SECTIONS

- *Type of study(ies):*
- *Objective/rationale (for each study):*
- *Indication(s) to be studied:*
- *Study design:*
- *Age group in which study(ies) will be performed:* INDICATE SPECIFIC AGE RANGE
- *Number of patients to be studied or power of study to be achieved:*
- *Entry criteria:* (i.e., INCLUSION/EXCLUSION CRITERIA)
- *Clinical endpoints, if appropriate:* NOTE PRIMARY EFFICACY ENDPOINT
- *Study evaluations:*
- *Drug information*
  - *dosage form:*
  - *route of administration:*
  - *regimen:*
  - *formulation:*
- *Safety concerns:*
- *Statistical information, including:*
  - *power of the study:*
  - *statistical analyses of the data to be performed:*
- *Labeling that may result from the study(ies):*
- *Format of reports to be submitted:* full study reports or analyses not previously submitted to the Agency addressing the issues outlined in this request with full analysis, assessment, and interpretation. INCLUDE OTHER INFORMATION AS APPROPRIATE
- *Timeframe for submitting reports of the study(ies):* THIS DATE MUST BE STATED

Please submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission “**PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY**” in large font, bolded type at the beginning of the cover letter of the submission. We recommend you seek a written agreement with FDA before developing pediatric studies. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Clearly mark your submission “**PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES**” in large font, bolded type at the beginning of the cover letter of the submission.

Reports of the studies should be submitted as a supplement to your approved NDA, a new drug application, or an amendment to your pending application with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the reports, clearly mark your submission **“SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED”** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked **“PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES”** in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter to develop additional pediatric information that may produce health benefits in the pediatric population.

If you have any questions, contact NAME, Project Manager, at PHONE NUMBER.

Sincerely yours,

OFFICE DIRECTORS SIGNATURE BLOCK

cc:

Archival NDA/IND ##-###

HFD-xxx/division file

HFD-xxx/PM-CSO

HFD-xxx/Team Leaders and Reviewers

HFD-xxx/Office Director

HFD-600/Office of Generic Drugs

HFD-2/MLumpkin

HFD-104/DMurphy

HFD-6/KRoberts

Drafted by:

Initialed by:

Final:

filename: <http://cdernet/pediatrics/WRLETTER.DOC>

PEDIATRIC WRITTEN REQUEST LETTER

INFORMATION REQUEST (IR)

## Attachment B

## Pediatric Written Request Checklist

NDA/IND# \_\_\_\_\_ Drug Product \_\_\_\_\_

<i>Have the following elements been addressed in the Written Request?</i> <b>Note: Highlighted areas must be completed</b>	YES	NO
Type of studies to be performed/submitted (check all that apply): <input type="checkbox"/> Clinical efficacy <input type="checkbox"/> Safety <input type="checkbox"/> Pharmacokinetic <input type="checkbox"/> Other (describe): _____		
Objective/rationale		
Indication to be studied		
Study design		
Age group(s) in which studies will be performed (if the age group(s) does not fall within the four defined age groups, check "Other" and specify the age range) <input type="checkbox"/> Neonate (0-1mos) <input type="checkbox"/> Infant (1 mos - 2 yrs) <input type="checkbox"/> Children (2-12 yrs) <input type="checkbox"/> Adolescents (12-16 yrs) <input type="checkbox"/> Other (state the ages): _____		
Number of patients to be studied or power of study to be achieved		
Entry criteria, i.e., inclusion/exclusion criteria		
Clinical endpoints, including proposed primary efficacy endpoint		
Study evaluations		
Drug information (dosage form, regimen(s), route of administration, and formulation)		
Safety concerns		
Statistical information, including, power of the study and statistical analysis to be performed		
Labeling that may result from the study(s)		
Format of the report to be submitted to the agency		
Timeframe for submitting the study reports (mo/da/yr) _____		

If "NO" is checked for any of the above, please attach an explanation.

cc:

Archival NDA/IND ##-###

HFD-xxx/division file

HFD-xxx/PM-CSO

HFD-xxx/Team Leaders and Reviewers

HFD-xxx/Office Director

HFD-2/MLumpkin

HFD-104/DMurphy

HFD-6/KRoberts

*<http://cdernet/pediatrics/wrcheck.PDF>*

PEDIATRIC WRITTEN REQUEST CHECKLIST

## Attachment C

## Sample Letter for Revisions to a Written Request for Pediatric Studies

NDA/IND APPLICATION NUMBER

SPONSOR

Attention: CONTACT, TITLE

ADDRESS

Dear CONTACT:

Reference is made to your correspondence dated DATE OF LETTER FROM SPONSOR REQUESTING CHANGES, requesting changes to FDA's DATE OF ORIGINAL PEDIATRIC STUDY REQUEST LETTER, Written Request for pediatric studies for GENERIC DRUG NAME.

We have reviewed your proposed changes and are amending the below listed sections of the Written Request. All other terms stated in our Written Request issued on DATE OF ORIGINAL PEDIATRIC STUDY REQUEST LETTER, remain the same.

INCLUDE ONLY THOSE SECTIONS THAT HAVE BEEN REVISED FROM THE ORIGINAL REQUEST

Reports of the studies that meet the terms of the Written Request dated DATE OF ORIGINAL PEDIATRIC STUDY REQUEST LETTER, as amended by this letter must be submitted to the Agency on or before DATE STUDY REPORTS DUE, to possibly qualify for a pediatric exclusivity extension under section 505A of the Federal Food, Drug, and Cosmetic Act.

Please submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission "**PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY**" in large font, bolded type at the beginning of the cover letter of the submission. We recommend you seek a written agreement with FDA before developing pediatric studies. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Clearly mark your submission "**PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES**" in large font, bolded type at the beginning of the cover letter of the submission.

Reports of the studies should be submitted as a supplement to your approved NDA, a new drug application, or an amendment to your pending application with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the reports, clearly mark your submission "**SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED**" in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked "**PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES**" in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter to develop additional pediatric information that may produce health benefits in the pediatric population.

If you have any questions, contact NAME, Project Manager, at PHONE NUMBER.

Originator: Deputy Center Director (Review Management)  
October 6, 1998

Sincerely yours,

OFFICE DIRECTORS SIGNATURE BLOCK

cc:

Archival NDA/IND ##-###

HFD-xxx/division file

HFD-xxx/PM-CSO

HFD-xxx/Team Leaders and Reviewers

HFD-xxx/Office Director

HFD-600/Office of Generic Drugs

HFD-2/MLumpkin

HFD-104/DMurphy

HFD-6/KRoberts

Drafted by:

Initialed by:

Final:

filename: *http://cdernet/pediatrics/REVWRLET.DOC*

REVISED PEDIATRIC WRITTEN REQUEST LETTER  
INFORMATION REQUEST (IR)

## Attachment D

## Sample Letter for Inadequate Proposed Pediatric Study Request

NDA/IND APPLICATION NUMBER

SPONSOR

Attention: CONTACT, TITLE

ADDRESS

Dear CONTACT:

Reference is made to your correspondence dated DATE OF SUBMISSION OF PROPOSED PEDIATRIC STUDY REQUEST FROM SPONSOR, requesting that FDA issue a Written Request under section 505A of the Federal Food, Drug, and Cosmetic Act for GENERIC DRUG NAME.

We have reviewed your proposed pediatric study request and are unable to issue a Written Request based on your submission.

We recommend you resubmit your proposed pediatric study request addressing all of the issues outlined below.

INCLUDE THOSE SECTIONS FROM ATTACHMENT B WHERE ADDITIONAL INFORMATION IS NEEDED

Please clearly mark your submission “**PROPOSED PEDIATRIC STUDY REQUEST**” in large font, bolded type at the beginning of the cover letter of the submission.

We look forward to working with you on this matter to develop additional pediatric information that may produce health benefits in the pediatric population.

If you have any questions, contact NAME, Project Manager, at PHONE NUMBER.

Sincerely yours,

DIVISION DIRECTORS SIGNATURE BLOCK

cc:

Archival NDA/IND ##-###

HFD-xxx/division file

HFD-xxx/PM-CSO

HFD-xxx/Team Leaders and Reviewers

HFD-xxx/Office Director

HFD-2/MLumpkin

HFD-104/DMurphy

HFD-6/KRoberts

Drafted by:

Initialed by:

Final:

filename: *http://cdernet/pediatrics/ialet.doc*

INADEQUATE PEDIATRIC STUDY REQUEST

INFORMATION REQUEST (IR)

Originator: Deputy Center Director (Review Management)

October 6, 1998

**Sample Pediatric Written Agreement****DATE**

The Food and Drug Administration and **SPONSOR** agree to the following terms for submitting pediatric studies:

**INSERT INFORMATION MAKING SURE TO ADDRESS ALL POINTS OUTLINED IN THE PEDIATRIC WRITTEN REQUEST AND ANY OTHER ELEMENTS OF THE PLANNED STUDY AGREED TO BY THE AGENCY AND THE SPONSOR.**

Any changes to this agreement should be made in writing by consensus under a separate correspondence. Alterations to this document without consensus are not valid.

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**SPONSOR'S SIGNATURE BLOCK**

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**OFFICE DIRECTOR'S SIGNATURE BLOCK**

CC:

Original 1 Archival IND/NDA ##-###

Original 2 Sponsor

HFD-xxx/division file

HFD-xxx/PM-CSO

HFD-xxx/Team Leaders and Reviewers

HFD-xxx/Office Director

HFD-600/Office of Generic Drugs

HFD-2/MLumpkin

HFD-104/DMurphy

HFD-6/KRoberts

Drafted by:

Initialed by:

Final:

filename: <http://cdernet/pediatrics/walet.doc>

PEDIATRIC WRITTEN AGREEMENT

GENERAL CORRESPONDENCE (GC)

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**Originator: Deputy Center Director (Review Management)**

**October 6, 1998**

Attachment F

**PEDIATRIC EXCLUSIVITY DETERMINATION CHECKLIST**

**PART I - TO BE COMPLETED BY THE REVIEWING DIVISION. UPON COMPLETION FORWARD TO THE PEDIATRIC EXCLUSIVITY BOARD, HFD-002.**

Date of Written Request from FDA \_\_/\_\_/\_\_. Application Written Request was made to: NDA/IND# \_\_\_\_\_

Timeframe Noted in Written Request for Submission of Studies \_\_/\_\_/\_\_.

NDA# \_\_\_\_\_ Supplement # \_\_\_\_\_ Circle one: SE1 SE2 SE3 SE4 SE5 SE6 SE7 SE8 SLR

Sponsor \_\_\_\_\_

Generic Name \_\_\_\_\_ Trade Name \_\_\_\_\_

Strength \_\_\_\_\_ Dosage Form/Route \_\_\_\_\_

Date of Submission of Reports of Studies \_\_/\_\_/\_\_.

Pediatric Exclusivity Determination Due Date (60 or 90 days from date of submission of studies) \_\_/\_\_/\_\_.

Was a formal Written Request made for the pediatric studies submitted?	Y ____	N ____
Were the studies submitted after the Written Request?	Y ____	N ____
Were the reports submitted as a supplement, amendment to an NDA, or NDA?	Y ____	N ____
Was the timeframe noted in the Written Request for submission of studies met?	Y ____	N ____
If there was a written agreement, were the studies conducted according to the written agreement? <div style="text-align: center;">OR</div> If there was no written agreement, were the studies conducted in accord with good scientific principles?	Y ____	N ____
Were the studies responsive to the terms of the Written Request?	Y ____	N ____

**FORWARD TO THE PEDIATRIC EXCLUSIVITY BOARD, HFD-002.**

**PART II - TO BE COMPLETED BY THE PEDIATRIC EXCLUSIVITY BOARD**

Pediatric Exclusivity	___ Granted	___ Denied
Existing Patent or Exclusivity Protection:		
<u>NDA/Product #</u>	<u>Eligible Patents/Exclusivity</u>	<u>Current Expiration Date</u>
_____	_____	_____
_____	_____	_____
_____	_____	_____

SIGNED \_\_\_\_\_ DATE \_\_\_\_\_

cc:

Archival NDA/IND ##-###

Originator: Deputy Center Director (Review Management)  
October 6, 1998

HFD-xxx/division file

HFD-xxx/PM-CSO

HFD-93/Division of Data Management Services

HFD-600/Office of Generic Drugs

HFD-2/MLumpkin

HFD-104/DMurphy

HFD-6/KRoberts

*<http://cdernet/pediatrics/EXCHECK2.PDF>*

PEDIATRIC EXCLUSIVITY DETERMINATION CHECKLIST